count (<150K/ul) was the only significant predictor when the analysis was restricted to NHL patients mobilized with chemotherapy (odds ratio 8.9, $p < 0.001$). Conclusions: A significant proportion (18%) of patients with NHL fails to mobilize stem cells. Use of filgrastrim without chemotherapy was associated with high failure rate, but this needs to be confirmed in a larger comparative study. For patients who were mobilized with chemotherapy, low platelet count is the most significant predictive factor.

Univariate Analysis in Patients with NHL

	N	N Failed	% Fail	OR[1]	95% CI[2]	p
Platelet Count						
<150 K	**34**	**14**	**41**			
≥150 K	**107**	**12**	**11**	**0.2**	**0.1–0.4**	**<0.001**
Cellularity						
<30%	**44**	**13**	**30**	**2.7**	**1.1–6.5**	**0.02**
≥30%	**97**	**13**	**13**			
Regimen						
Ifos/VP16	**96**	**12**	**13**			
G-CSF alone	**13**	**8**	**62**	**11.2**	**3.1–40**	**<0.001**
Cyclophosphamide	**14**	**3**	**21**	**1.9**	**0.5–7.8**	**0.4**
Other	**18**	**3**	**17**	**1.4**	**0.3–5.6**	**0.6**

[1]Odds Ratio.
[2]Confidence Interval.

97

POSITRON EMISSION TOMOGRAPHY IDENTIFIES A DIFFERENTIAL PATTERN OF BONE MARROW FDG UPTAKE IN "POOR" AND "GOOD" PERIPHERAL STEM CELL MOBILIZERS

Marcacci, G.[1], Caracò, C.[2], D'Arena, G.[1], Aloj, L.[2], Corazzelli, G.[1], Frigeri, F.[1], Lastoria, S.[2], Pinto, A.[1] [1]National Cancer Institute "Fondaz. Pascale", Naples, Italy; [2]National Cancer Institute "Fondaz. Pascale", Naples, Italy.

The use of prophylactic G-CSF is associated to the increase of bone marrow (BM) fluorodeoxyglucose (FdG) uptake as detected by Positron Emission Tomography (PET). In contrast, no data is available as to changes in BM FdG-uptake during peripheral blood stem cell (PBSC) mobilization. This study was aimed at investigating patterns of BM FdG uptake during mobilization as quantified by Standardized Uptake Value (SUV) determinations. We also evaluated whether PET scanning may turn of value for identifying *good* and *poor* mobilizers. To our knowledge this is the first PET-based study in this setting. *Methods* Seventeen patients(pts)(M/F = 10/7), median age 51 yrs (r 28–65), with relapsed lymphoma (NHL/HD = 13/4) without BM involvement, were accrued after informed consent. Baseline PET was obtained at relapse, before salvage therapy and any CSF administration. After salvage regimes pts were mobilized by VRL/CTX or ARA-C; G-CSF (10 μg/kg/d) was given from day +6 through apheresis. PET scans were obtained on day +9 or +10 (after nadir with a WBC > 1000/μl). SUVmax and average (avg) were measured (whole lumbar spine and bilateral iliac regions) and compared to SUV of the same BM regions at baseline PET. The aim was to calculate a BM specific Δ-SUV (mobilizing *vs* steady-state Δ-SUV) for each single patient. *Results* Twelve pts mobilized PBSC (median CD34 peak 39.99/μl, r 23.28–280.58/μl; median CD34 in the harvest 3.3×10^6/Kg, r 2.1–12.5) while 5 pts were *poor* mobilizers (median CD34 peak 10.9/μl, r 7.5–14.1/μl). In the group of *good* mobilizers, apheresis was performed at CD34 peak (day +11,+14), with a median of 1 apheresis/pt (r 1–2). Unexpectedly, effective mobilization was associated with a low BM uptake of FdG: median BM Δ-SUVmax and Δ-SUVavg of 2.0 (r 1.0–3.8) and 2.3 (r 0.9–3.9), respectively. In contrast, *poor* mobilizers displayed a median Δ-SUVmax and Δ-SUVavg of 4.7 (r 2.4–12.8) and 5.9 (r 4.1–14.2), respectively.

Conclusions: While FdG-BM uptake usually increases upon CSF administration, our results suggest that PBSC mobilization may be associated with a more complex metabolic pattern of BM as detected by PET. We documented that, 48 to 72 hrs before CD34 peak, *poor* mobilizers display a higher FdG-BM uptake (Δ-SUV > 3) as compared to *good* mobilizers (Δ-SUV < 3). These preliminary results indicate that BM PET may represent a new tool for early identification of *poor* mobilizers allowing a timely modification of the mobilization strategy to possibly rescue the procedure.

98

RADIO-IMMUNOTHERAPY FOR LOW GRADE NON-HODGKIN'S LYMPHOMA MAY IMPAIR THE ABILITY TO MOBILIZE AUTOLOGOUS PERIPHERAL BLOOD STEM CELLS

Raptis, A., Mapara, M., Bilodeau, A., Hornyak, M., Agha, M.E. UPMC Cancer Centers/University of Pittsburgh Medical Center, Pittsburgh, PA.

High dose chemotherapy and autologous stem cell transplantation (ASCT) is a proven effective treatment modality for patients with relapsed non-Hodgkin's lymphoma. Radioimmunotherapy (RIT) with ^{90}Y-ibritumomab tiuxetan has been shown to be useful in patients with relapsed NHL, but is now being used in the upfront setting for patients with low grade NHL, as some protocols now offer abbreviated chemotherapy courses followed by RIT. As patients relapse high dose therapy and ASCT become a valuable option but the effect of RIT on the stem cell collection becomes an important issue. We report four patients with follicular NHL who relapsed within 6–8 months after RIT were treated with salvage chemotherapy then mobilized with Cyclophosphamide and G-CSF. Two patients were heavily pre-treated for multiple relapses, but two had only one relapse following upfront RIT. Only 2/4 patients mobilized successfully, but with low yield. One of the patients developed secondary leukemia, 6 months after ASCT. Surprisingly, the mobilization failure patients were young, not heavily treated (had 6–7 cycles of chemotherapy including the upfront and salvage therapy), no exposure to external beam radiotherapy, but had heavy tumor burden at initial presentation. Our results suggest that mobilization failure following RIT is much higher that would have been predicted. Caution should be exercised when offering RIT to patients with bulky disease low grade lymphoma as part of the upfront therapy, as rapid relapses may not be salvageable with high dose therapy, given the high rate of mobilization failure even in patients who are not heavily treated. The long term safety of RIT and myelodysplasia in such patients is also an important concern, given the short interval of tAML in our patient.

99

PREDICTORS OF OUTCOME OF MANTLE CELL LYMPHOMA IN PATIENTS WITH PROGRESSIVE DISEASE FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT)

Al-Farsi, K., Nagy, T., Keating, A., Crump, M., Kuruvilla, J. Princess Margaret Hospital, Toronto, ON, Canada.

Introduction: Mantle Cell Lymphoma (MCL) is a subgroup of malignant lymphomas that is considered incurable with conventional therapy. While ASCT has improved progression free survival (PFS), relapse remains a major issue. For patients (pts) who relapse after ASCT, there is little information on the predictors of outcome and optimal treatment strategy. We reviewed pts with progressive disease following ASCT in an attempt to identify predictors of subsequent outcome. **Method:** We retrospectively reviewed our computerized database and charts of pts undergoing ASCT from May 1987 - Jul 2006. Of 47 pts, 21 relapsed after ASCT; 20 had adequate data on subsequent therapy and were analyzed for factors influencing progression free survival (PFS) and overall survival (OS) using Kaplan-Meier and Cox-Proportional Hazards analyses. **Results:** Pt characteristics: At relapse post-ASCT, median age was: 56 years (range 40–69). Stage 3 or 4: 16. High LDH: 8. Disease status of ASCT: CR1/PR1 = 9, >CR1/PR1 = 11. IPI scores: low (n = 9), low-intermediate (n = 8), high-intermediate (n = 2) and high (n = 1). FLIPI scores: low (n = 10), intermediate (n = 4) and high (n = 6). Seven had bone marrow involvement, 3 had involvement of peripheral blood and 5 had splenomegaly. Eighteen pts received subsequent treatment: R-FCM: 4, Rituximab: 1, Radiation

alone: 3, other combination chemotherapy: 9 and 1 underwent reduced intensity allogeneic transplantation. Two pts were not fit to receive further treatment and had rapidly progressive disease (PD). Of the treated pts, 6 achieved CR (4 subsequently progressed), 5 PR and 7 had PD. Eleven pts remain alive (only 2 in CR) with PD accounting for all deaths. With a median follow-up of 31 months (m) post relapse for living pts, median PFS from the time of relapse post-ASCT was 5 m and OS was 34 m. No significant predictors of PFS could be identified. For OS, univariate analysis identified time to relapse (TTR; $p = 0.011$), performance status (PS; $p = 0.010$) and total IPI score ($p = 0.041$) as being statistically significant. Only TTR remained significant on the multivariate model. TTR less than 12 months portends a very poor outcome (2 year OS 0% compared to 62% form TTR >12 m; $p < 0.001$). **Conclusion:** Pts with MCL who relapse after ASCT do poorly, especially those relapsing within one year of ASCT. New therapeutic approaches incorporating maintenance therapy post-ASCT or the use of novel agents such as bortezomib or mTOR inhibitors should be explored in this group.

100

FLUID RELATED COMPLICATIONS WITH FILGRASTIM (G-CSF) 10 MCG/KG ONCE DAILY VERSUS 5 MCG/KG TWICE DAILY IN AMYLOIDOSIS PATIENTS UNDERGOING PERIPHERAL BLOOD STEM CELL MOBILIZATION

Perreault, S.K.[1], Burzynski, J.A.[1], Hoskin, T.L.[2], Leung, N.[3], Buadi, F.K.[3], Dispenzieri, A.[3], Hayman, S.R.[3], Kumar, S.K.[3], Lacy, M.Q.[3], Gertz, M.A.[3], Wolf, R.C.[1] [1]Mayo Clinic, Rochester, MN; [2]Mayo Clinic, Rochester, MN; [3]Mayo Clinic, Rochester, MN.

Background: High dose melphalan followed by peripheral blood stem cell (PBSC) transplantation is an established therapy for AL amyloidosis. One limitation is the frequent fluid related complications that occur during PBSC mobilization (Blood 2004:1143a). The development of fluid related complications during mobilization predicts decreased survival after PBSC transplant (Blood 2005;106:3353). At Mayo Clinic, G-CSF 10 mcg/kg once daily was the standard until 2004. In attempt to reduce fluid related complications the practice changed to G-CSF 5 mcg/kg twice daily in July 2004. It is unknown if this change impacted the incidence of fluid related complications during PBSC mobilization. **Methods:** We conducted a retrospective evaluation of patients with amyloidosis undergoing PBSC mobilization at Mayo Clinic. Following IRB approval, patients were identified by reviewing the Mayo Clinic dysproteinemia data base and data extracted from the medical record. Forty-six patients from the once daily and 22 patients from the twice daily were excluded due to use of mobilization agents in addition to G-CSF, second mobilization, syngeneic transplant or consent refusal. A fluid related complication was defined as new peripheral edema, pleural effusion or ascites, or initiation of supportive therapy (diuretics, albumin, or dopamine) to promote diuresis. **Results:** From 7/98 to 8/03, 123 patients received once daily G-CSF. From 7/04 to 8/07, 182 patients received twice daily G-CSF. Organ involvement was similar in both series; single organ (43% vs 36%; $p = 0.2$), two organs (38% vs 62%; $p = 0.5$) and 3 or more organs (22% vs 26%; $p = 0.5$). Most patients had either kidney involvement (65% vs 71%; $p = 0.2$) or heart involvement (51% vs 57%; $p = 0.3$). Baseline edema (61% vs 53% ($p = 0.06$)) and baseline diuretic use (58% vs 55% ($p = 0.7$)) was similar in both groups. Fluid related complications occurred with similar frequency regardless of administration schedule, 50% vs 51% ($p = 0.9$). Two patients in the once daily and 4 patients in the twice daily administration died prior to PBSC transplant. In patients that received a PBSC transplant, survival was similar at day 100; 88% vs 92% and one year; 83% vs 88% ($p = 0.6$). **Conclusion:** Changing from once daily to twice daily G-CSF administration in patients with amyloidosis did not impact the incidence of fluid related complications or mortality at day 100 or one year after PBSC transplant.

Comparison of Complications based on G-CSF Schedule of Administration

	Once daily Filgrastim n = 123 N (%)	Twice daily Filgrastim n = 182 N (%)	p value
Fluid Complications	**63 (50)**	**93 (51)**	**0.9**
Hospitalization	**28 (23)**	**24 (13)**	**0.03**
Hospitalization related to fluid complication	**21 (17)**	**10 (5)**	**0.001**
Diuretic adjustment needed	**42 (34)**	**89 (49)**	**0.012**
Non-pharmacological intervention*	**10 (8)**	**9 (5)**	
Death prior to PBSC Transplant	**2 (1.6)**	**4 (2.2)**	
Patient did not undergo PBSC transplant	**9 (7.3)**	**37 (20)**	

*Thoracentesis, Paracentesis, Hemodialysis, Pleurodesis, and Mechanical Ventilation.

101

PHASE II TRIAL EVALUATING APREPITANT (AP) FOR PREVENTION OF NAUSEA AND VOMITING SECONDARY TO HIGH-DOSE CYCLOPHOSPHAMIDE (CY) ADMINISTERED TO PATIENTS UNDERGOING AUTOLOGOUS (A) PERIPHERAL BLOOD PROGENITOR CELL (PBPC) MOBILIZATION

Abidi, M.H.[1,2], Abrams, J.[1,2], Ibrahim, R.[3], Ayash, L.[1,2], Cronin, S.[3], Al-Khadimi, Z.[1,2], Lum, L.[1,2], Ratanatharathorne, V.[1,2], Uberti, J.[1,2] [1]Wayne State University, Detroit, MI; [2]Barbara Ann Karmanos Cancer Center, Detroit, MI; [3]Eugene Appelbaum College of Pharmacy and Allied Health Professions, Detroit, MI.

Background: Adequate PBPC mobilization in the range of 2–5 $\times$ 10^6 $CD34^+$ cells/kg body weight is a prerequisite for administration of high-dose chemotherapy and A-PBPC transplant. Cy and filgrastim combination provides a better PBPC yield as compared to filgrastim, which has a failure rate of 15–20%. In this setting, high-dose Cy is associated with significant nausea and vomiting. Ap is a new antiemetic that is a Neurokinin-1 receptor antagonist and may reduce the incidence of this side effect. We have conducted a phase II trial evaluating efficacy and safety of adding Ap to standard antiemetic combination of 5-HT3 antagonists and adjusted dose of corticosteroids. Primary objective of this study was the control of acute vomiting without the use of rescue medications at 24 hours post Cy. The data of the first interim report are presented. **Methods:** From May 2005 to May 2007, 22 pts were enrolled, four of whom are not evaluable for response. Three pts did not receive Ap; one withdrew consent after a single dose. All received Cy 4 gm/m^2 and filgrastim (10–16 mcg/kg/d) for stem cell mobilization. Granisetron 1 mg, dexamethasone 10 mg and Ap 125 mg was administered orally 1 hour before Cy followed by Ap 80 mg once daily $\times$ 2 days. This study used Simon's optimal two-stage design constrained to fewer than 40 pts with 10% type I error and 85% statistical power. Ap is considered effective if it prevents nausea and vomiting in at least 65% of patients. Ap is judged ineffective if the rate of vomiting control was 45% or less. **Results:** Ten (55%) of 18 response-evaluable pts had no vomiting episodes and received no rescue medications during the first 24 hours following Cy. Of those who did not achieve the primary endpoint, four pts reported no vomiting episodes but received rescue medications. The other four pts had at least one vomiting episode and one received rescue anti-emetic. Ten pts had no delayed vomiting (25–120 hrs). Ten pts reported no nausea in 24 hours and five pts experienced mild nausea. Only 6/18 (33%) pts experienced moderate to severe delayed nausea (25–120 hrs). No toxicities related to Ap were noted for any patients. All pts had adequate mobilization of stem cells (median $CD34^+$: 7.57 $\times$ 10^6/kg) and proceeded to A-PBPC transplant. **Conclusion:** The results of this interim analysis justify continuation to stage 2 with enrollment of 17 more patients. Ap has potential to effectively control nausea and emesis in pts receiving high-dose Cy.